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A community study in Cornwall UK of sudden unexpected death in epilepsy (SUDEP) in a 9-year population sample

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ABSTRACT

Purpose: Epilepsy-related death, particularly sudden unexpected death in epilepsy (SUDEP), is underestimated by healthcare professionals. One argument that physicians use to justify the failure to discuss SUDEP with patients and their families is that there is a lack of evidence for any protective interventions. However, there is growing evidence of potentially modifiable risk factors for SUDEP; although large-scale trials of interventions are still lacking. We determined the main risk factors associated with SUDEP in a comprehensive community sample of epilepsy deaths in Cornwall UK from 2004 to 2012.

Methods: We systemically inspected 93 cases of all epilepsy and epilepsy associated deaths which occurred in Cornwall between 2004 and 2012 made available to us by the HM Cornwall coroner. These are the deaths where epilepsy was a primary or a secondary cause.

Results: 48 cases met the criteria for SUDEP and we elicited associated relevant risk factors. Many findings from our study are comparable to what has been reported previously. New points such as most of the population had increase in either or both seizure frequency/intensity within six months of death and majority did not have an epilepsy specialist review in the last one year to demise were noted.

Conclusion: This study is the first epidemiological study in England occurring in a whole population identifying systemically all deaths and the first large scale review in UK of SUDEP deaths since 2005. Being a community based study a key issue which was highlighted was that in the SUDEPs examined many might have been potentially preventable.

1. Introduction

Epilepsy-related death, particularly SUDEP, is underestimated by healthcare professionals.[1] One argument that physicians use to justify the failure to discuss SUDEP with patients and their families is that there is a lack of evidence for any protective interventions. However, there is growing evidence of potentially modifiable risk factors for SUDEP; although large-scale trials of interventions are still lacking. We determined the main risk factors associated with SUDEP in a comprehensive community sample of epilepsy deaths in Cornwall from 2004 to 2012. We used many of the clinical risk factors identified in the Cornish SUDEP safety checklist to collect data in a structured manner.[2,3]

We compared the risk factors identified by literature review from different studies against those identified in this new cohort of SUDEP deaths.

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Table 1
SUDEP: definition and criteria (Annegers, 1997).[5,6]

1	The victim suffered from epilepsy, defined as recurrent unprovoked seizures
2	The death occurred suddenly (in minutes), when known
3	The victim died unexpectedly, while in reasonable state of health
4	Death occurred during normal activities and benign circumstances
5	An obvious medical cause of death was not found
6	Death was not directly caused by a seizure or status epilepticus

Definite = all 6 and autopsy, Probable = all 6, SUDEP autopsy not performed but no other explanation, Possible = all 6, SUDEP Autopsy not performed and there could be an alternate explanation

2. Methods

The Cornwall coroner's office has a computerized system with a search engine to explore all registered death certificates. The data were collected from the coroner's records using the terms 'ep', 'epilepsy', 'Seizures', 'fits', 'Sudden death' and 'SUDEP' in either part 1 or 2 of the death certificate. Ninety three deaths were thus identified by the coroner's office. Each death's case file was reviewed to ascertain those deaths which met the SUDEP criteria and classification, provided by Nashef[4] and Anneger[5,6] (Table 1).

Of the 93 cases of epilepsy related deaths which occurred in Cornwall between 2004 and 2012, 48 cases met the criteria for SUDEP (Table 2 details subtypes). We applied the clinical risk factors from our previously developed SUDEP checklist with other relevant dimensions (last review by specialist, GP etc.) to these deaths[2,3] (detailed in Table 3).

We cross-referenced epilepsy deaths of these years with public health data on epilepsy deaths held by the Public Health Department of Cornwall and the Isles of Scilly Primary Care Trust. The public health data showed 73 epilepsy deaths (43 males and 30 females) for the period of 2006–2012. This is in keeping with our estimates for that period. The public health data only had the year, number of deaths and sex recorded.

95% confidence intervals were calculated using a binomial calculation, making no a prior assumptions about the population distribution.

3. Results

The United Kingdom (UK) has a population of about 60 million. Cornwall is a county in UK with a population of 550,000 (about 1% of the UK population). It is largely a rural county and not subject to major immigration/emigration (except for large number of tourists during summer). The incidence of SUDEP has been estimated as 0.1% of all people diagnosed with epilepsy per year. An estimated 500 deaths occur in a year due to SUDEP in the UK[7] and thus Cornwall would be expected to have 5 SUDEP deaths/year. Our study is consistent with these numbers as 48 deaths over 9 years represent a rate of 5.33 SUDEP deaths/year.

Table 2
Breakdown of the 48 cases to SUDEP subtype.

Definite	Probable	Possible
31	9	8

Among the 48 cases, the mean age was 42.5 years (range 2–82 years). The median and mode were respectively 42 and 46 years respectively. There were more males (33) than females (15), 68.8% ± 13.1 (mean and 95% confidence intervals). Early age of onset of epilepsy (less than 15 years age) was present in 33 cases, 74.4 ± 13%.

34 People had more than a 15-year history of epilepsy, (77.3 ± 12.4%, data was not available in 5 cases). Unclear treatment history was found in 31 cases, 66.0 ± 13.5%. 39 subjects had suffered from tonic clonic epilepsy (type of epilepsy not available in 5 cases), 91.0 ± 9.0%. It was not possible to determine the syndromic diagnosis of the epilepsy with the information available. Increasing seizure frequency and severity, documented in family/partner and GP reports, in 3–6 months prior to death was seen in 91.3 ± 8.1%. Only 19.1 ± 11.2% had contact with specialist services compared to 51.2 ± 15.3% having contact with GP services in the preceding year: 81.4 ± 11.6% had died in prone position. Night surveillance was present in only 3 cases with the majority (43) not having night surveillance (93.5 ± 7.1%).

Other significant results included compliance issues for 55 ± 15.4% and alcohol problems in 46.5 ± 14.9%. Compliance concerns were picked out from the records by the researchers based on reading through reports of the GP, family, partner etc. where these have been mentioned in the provided evidence.

History of depression and use of anxiolytic medication was present in 11 cases, 26.8 ± 13.5%.

Other key findings are summarized in Table 3.

4. Discussion

The findings from our study are comparable to what has been reported in previous studies and consistent with our literature

Table 3
Key findings.

Risk factor	Missing data	*N* (total 48) (% allowing for missing data)
Male[a]	0	33 (69)
Mean age at death (yrs)	0	42.5
Diagnosis of tonic clonic epilepsy[a]	5	39 (91)
Onset of epilepsy before age 15 yrs[a]	5	33 (74)
>15 yr duration of epilepsy[a]	5	34 (77)
Increasing seizure frequency/severity 3–6 months prior to death[a]	4	42 (91)
3 or more AEDs prescribed	4	5 (11)
Unclear treatment history[a]	1	31 (66)
Compliance issues[a]	7	22 (55)
Frequent AED changes in preceding year[a]	2	9 (20)
Sub therapeutic AED levels[a]	15	16 (48)
Contact with GP in preceding 12 months	7	21 (51)
Contact with specialist services in preceding 12 months	1	9 (19)
Presence of night surveillance[a]	2	3 (6)
Death in prone position[a]	5	35 (81)
Presence of Intellectual Disability[a]	2	3 (7)
Alcohol Misuse[a]	5	20 (47)
Treatment for Depression and use of anxiolytic medication[a]	7	11 (27)

[a] These items are a part of the SUDEP safety checklist.

review.[2] The non-modifiable risk factors that were more frequent include male gender, younger age of onset and longer duration of epilepsy. The potential modifiable risk factors that were more frequent included uncontrolled seizures (especially tonic clonic seizures), recent increase and/or high seizure frequency, unclear treatment/non-compliance history, absence of night surveillance and prone position, psychiatric comorbidity including depression, being on anxiolytic medication and alcohol misuse. It is worth recognizing that although these factors are potentially modifiable, it may be challenging for a patient to change these. Moreover, some patients remain pre-disposed to poor seizure control in spite of the best efforts of the individual and the treating team. Nevertheless, our data support the better management of comorbid mental health problems by those managing people with epilepsy.

Unlike most other studies on SUDEP which are done on select populations or in tertiary care/specialist centers, our study subjects were drawn from a fairly stable general population and these figures can be used to calculate the incidence in the general population of Cornwall.

The fact that only 9 of patients had definitely met a specialist 1 year prior to death and 21 had contact with the GP for an epilepsy medication review raises important questions about the organization and delivery of services. Mechanisms such as GP drop in clinics, outreach services or telehealth services may be needed to contact those who lose contact with health services or those who are having an increase in seizures in community. The GPs also may benefit from education about the risk of SUDEP and the importance of referral to specialist services esp. when risk factors for SUDEP are present. It is possible that the risk factors be considered for use for screening in primary care to identify change in seizure patterns and associated factors. This is especially relevant because 42 of the SUDEP sample had a clinically identifiable increase in seizure intensity and/or frequency 3–6 months prior to death.

Non surveillance of seizures and sleeping in the prone position, especially when there is a noticeable change in the clinical picture appears as a possible significant modifiable risk factor. A combined action by health and social services along with patient/carers using optimum efforts to control seizures and nocturnal monitoring may minimize the risk of SUDEP.

Cornwall has a specialist service for people with Intellectual Disability (ID) and epilepsy which is rare in the UK. Only 3 people with clinical ID were identified of the 48 SUDEP deaths, none of whom were known to the ID specialist epilepsy service. Kiani et al. studied SUDEP and ID whilst utilizing the Leicestershire Intellectual Disability Register database between 1993 and 2010.[8] 26 people with ID died from probable or definite SUDEP, which was the second most common cause of death among adults with ID and epilepsy. During the same study period, 83 adults without ID had died of probable or definite SUDEP. This contrasts greatly with Cornwall, as of all SUDEP deaths in Cornwall only 6.25% had a learning disability, whereas in Leicestershire 23.4% suffered from an ID. In the Leicester study, the SMRs for SUDEP in patients with ID were 37.6 for men (95% CI: 21.9–60.2) and 52.0 for women (95% CI: 23.8–98.8). It is possible that having a specialist epilepsy service for patients with ID may save lives. The demography of Leicester, other service designs and individual patient details could have a bearing on this finding.

Psychiatric comorbidity including depression, anxiety and alcohol misuse are also important modifiable risk factors. A close liaison between epilepsy and mental health services can possibly reduce the risk of SUDEP in this vulnerable population. There appears to be high representation of people with depression and anxiety (27%). This is consistent with the findings of the recent study by Fazel et al. which has found higher rates of psychiatric comorbidity in premature deaths in patients with epilepsy.[9] These findings are also consistent with Ridsdale et al. finding of recorded alcohol problems, (OR = 2.96) and depression (OR = 1.39) being a higher risk factor for mortality in epilepsy in general population.[10]

5. Weakness and strengths of the study

We appreciate that a few deaths missed could influence the hypothesis drawn and outcomes presented. We corroborated our population with Public Health data in Cornwall. We compared the annual deaths year by year but due to the fact that the coroner's data was available only after inquest which could take place up to 2 years after a death there were minor differences in numbers. Notwithstanding these issues, this data support that we have captured most if not all the deaths recorded.

It is clear to the researchers that some diagnosis recorded as 'epilepsy' in the coronial records was 'SUDEP'. We included those deaths which met the criteria of SUDEP. Unfortunately there were some records which had limited data in them and no post mortem and the diagnosis offered by the coroner thus could not be

Table 4
Data used from tables modified from Monte et al. (2007)[12] and Surges et al. (2009).[13]

Study	Study population	SUDEP/all deaths (where available)
Langan (2005)[11]	Retrospective case–control study, multiple sources, age and geography matched	154
Hughes (2009)[14]	Case–control study	91
Lear-kaul et al. (2005)[15]	All cases of autopsy with SUDEP from Arapahoe County Coroners (1993–2000) and Denver Office of the Medical Examiner (1996–2000)	67
Hitiris et al. (2007)[16]	Retrospective case–control study in an epilepsy centre	62
Nilsson et al. (1999)[17] and Nilsson et al. (2001)[18]	Hospital discharge registry and population based prospective cohort study	57
Our study	Community study includes all cases of inquest of epilepsy deaths between 2004 and 2012 in Cornwall UK	48/93
Lip and Brodie (1992)[19]	Specialist centre	12/18
Racoosin (2003)[20]	AED trails	52/142
Kloster (1999)[21]	Tertiary Referral centre	37/140
Nashef et al. (1998)[22]	Self referral of relatives of patients of SUDEP	26/34
Leestma et al. (1997)[23]	Lamotrigine clinical data base	24/45
Derby[24]	Refractory AED registry	15/63
Nasheff et al. (1995)[25]	Residential school for ID students	14/20
Walczak et al. (2001)[26]	Prospective cohort at a specialist referral center	20
Williams et al. (2006)[27]	Prospective case control study of patients on specific AEDs	16
Timmings et al. (1993)[28]	Retrospective case audit study in an epilepsy unit	14
Antoniuk et al. (2001)[29]	Retrospective review of 15,001 death certificates registered at Medico legal Institute of Curitiba from 1990 to 1999	20/53
McKee and Bodfish (2000)[30]	Only ID cases	11
Beran et al. (2004)[31]	Epilepsy clinic	21

reviewed. It appears that as the awareness of SUDEP grew more deaths with epilepsy links were referred for a SUDEP autopsy and a full inquest.

The data recorded was a collection of reports as felt appropriate by the coroner in order to help her in her inquest proceedings. Thus in certain cases data is inconsistent (due to conflicting reports by the observers such as family, paramedics etc.), unavailable (for example GP reports not mentioning when the last epilepsy review happened, if there had been a specialist referral or the GP report itself being not available). Evidencing this has been left to the data collectors' judgment. Attempts were made to keep data collection consistent with the data collectors being trained in SUDEP risk factors and any ambiguous data being discussed with the full group of researchers.

This study is the first epidemiological study in a community setting in England and the first large scale review of SUDEP deaths since the SENTINEL Audit in 2002[1] and Langan (2005).[11] This is the 7th largest study as per SUDEP cases collected (Table 4) and has looked at the complete population trends and not relied only on referrals as many other studies did.

The study highlights the need for a consistent and homogenous pattern of collection esp. given the difficulty of data collection and rarity of outcome to help pool gathered data from different studies. It suggests a potential association between the cumulative effects of risk factors, the way services are designed and the possibility that SUDEP might not be as 'Sudden' as we think it to be.

6. Conclusion

This is a survey of SUDEP deaths in England covering a defined population across 9 years and believe it is one of the largest such study in England especially from a community non-hospital perspective. Our findings are largely consistent with other similar studies. A point of interest is that it appears in the population which died, engagement with clinical services at the right time when there was a noted deterioration in core epilepsy factors, social factors, psychological factors and other biological factors leading to a possible cumulative increase in risk was inadequate. Further studies are needed to establish this further and we hope to compare the data from the deaths in this research study with equivalent control cases for people with epilepsy who have not died from SUDEP.

Conflict of interest statement

No known conflict of interest exists for any of the authors involved in this manuscript.

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